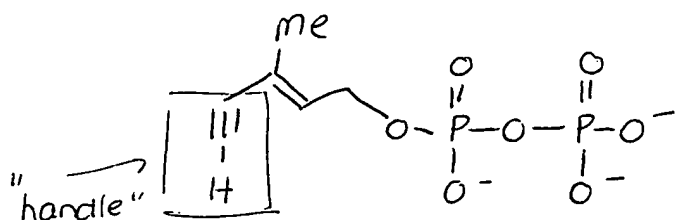
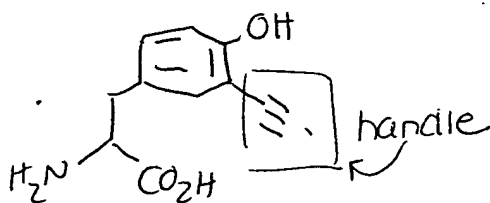
[illegible]

Essential Starter units (w/ functional handles)

① Terpene-based pathway



② Amino-acid based pathway



③ Polyketide pathway

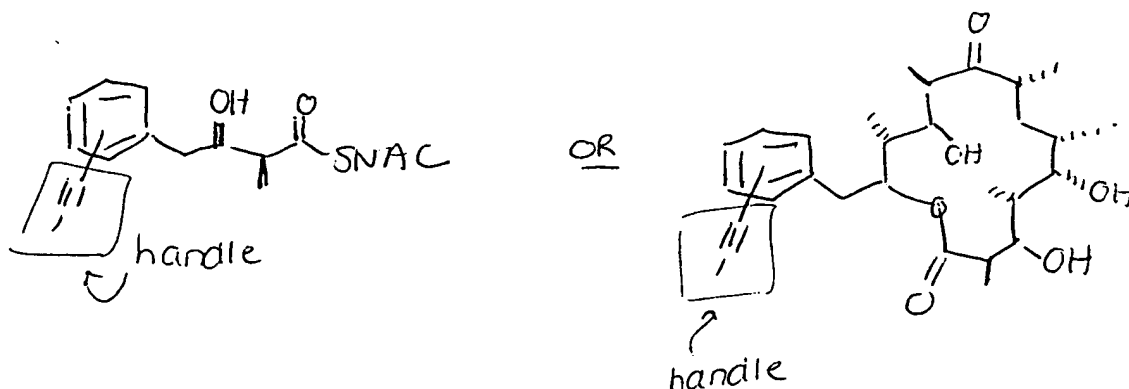


Figure 2

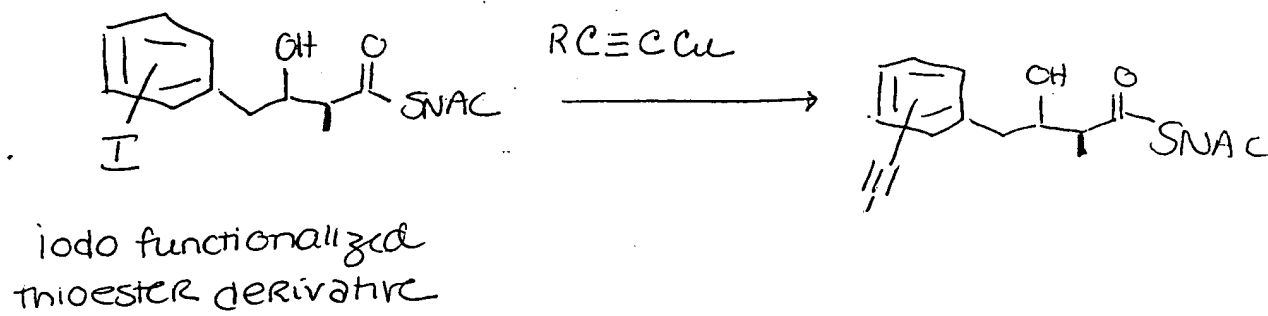


Figure 3

Combinatorial Biology

Modular Biosynthetic Enzymatic machinery

Genetic manipulation

(B) Attach starter units having "handles" to solid phase first via Glaser coupling, for example, to obtain a support bound starter unit, e.g. $[S]-\equiv-\equiv-SS$

(A) Feed starter units with "handles" e.g. $[S]-\equiv-$

Mutated Biosynthetic Pathway

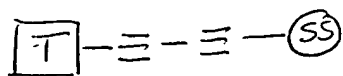
INVIVO OR INVITRO

INVIVO OR INVITRO

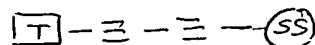
Either:
(1) Feed directly into mutated pathway OR
(2) "Combinatorialize" the support bound starter units and feed into mutated pathway

optionally expose to biosynthetic pathway again until a desired structure is obtained

through machinery: starter unit transformed into a complex template



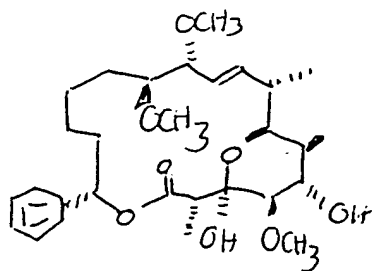
through machinery: starter unit transformed into a complex template
• can also diversify using parallel methods
• attach to solid phase



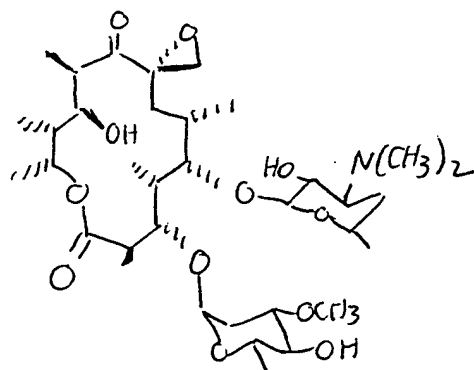
diversification using split-pool organic synthesis

collection of "unnatural" natural products

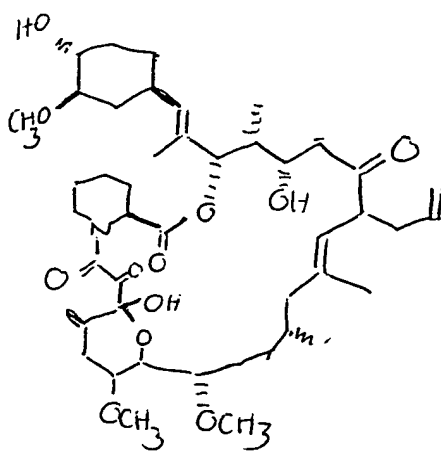
FIGURE 4



Soraphen(A)



Oleandomycin



FK 506

Figure 5